Response to Letter Regarding Article, “Effects of the Antianginal Drugs Ranolazine, Nicorandil and Ivabradine on Coronary Microvascular Function in Patients with Non-obstructive Coronary Artery Disease: A Meta-analysis of Randomized Controlled Trials”

Dear Dr. Shader,

We thank Dr. Tolunay for expanding our point regarding the effect of ranolazine on chest pain in patients with coronary microcirculation dysfunction from our recent meta-analysis (Effects of the Antianginal Drugs Ranolazine, Nicorandil, and Ivabradine on Coronary Microvascular Function in Patients With Nonobstructive Coronary Artery Disease: a Meta-Analysis of Randomized Controlled Trials). Dr. Tolunay mainly offers the following two points: (1) the improvement of angina pectoris by ranolazine may be due to the reduction of pain caused by brain effect; and (2) a large dose of ranolazine will produce many adverse reactions.

To the first point, results of our meta-analysis showed that ranolazine can improve indicators of coronary microcirculation dysfunction, including coronary flow reserve and myocardial perfusion reserve index. Therefore, from the perspective of monism, ranolazine can alleviate the symptoms of microvascular angina pectoris by improving the blood supply of the myocardium. However, as a late sodium channel blocker, ranolazine can block many sodium channel subtypes, such as Na, 1.7, 1.8, and so forth, which are related to hyperalgesia. Thus, we also agree that ranolazine may have a direct pain relief effect by increasing the pain threshold. It is therefore possible for ranolazine to play a role in improving Seattle Angina Questionnaire scores through a variety of mechanisms.

To the second point, we believe that there is a dose treatment window for any drug, and exceeding this dose will result in more, or more serious, adverse reactions than the treatment dose. At present, the adverse reactions of clinical doses of ranolazine are nonfatal, and most patients find them tolerable. We therefore believe that the side effects of ranolazine at the therapeutic dose are acceptable. In addition, there is a question about whether the withdrawal of ranolazine will lead to the withdrawal reaction similar to amphetamine, i.e. whether ranolazine will cause addiction. First, ranolazine may only have one tenth of the effect of the amphetamine. Second, there is no study showing that such an adverse reaction of ranolazine occurs. Thus, the current evidence shows that the use of ranolazine does not lead to addiction. Finally, we also agree that long-term and large-scale clinical and follow-up trials should be completed to further evaluate the effects and adverse reactions of ranolazine.

DISCLOSURES
None.

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REFERENCES


